

**Supplementary Table 1.** Best overall response per BIRC by PD-L1 expression in all treated patients and TMB-evaluable patients

	All treated patients <i>N</i> = 270				TMB-evaluable patients <i>n</i> = 139	
Response	PD-L1 <1% <i>n</i> = 146	PD-L1 ≥1% <i>n</i> = 124	PD-L1 <5% <i>n</i> = 187	PD-L1 ≥5% <i>n</i> = 83	PD-L1 <1% <i>n</i> = 69	PD-L1 ≥1% <i>n</i> = 70
Objective response rate, % (95% CI)	16.4 (10.8–23.5)	25.8 (18.4–34.4)	16.0 (11.1–22.1)	31.3 (21.6–42.4)	18.8 (11.4–29.6)	24.3 (15.8–35.5)
Best overall response, <i>n</i> (%)						
Complete response	6 (4.1)	12 (9.7)	8 (4.3)	10 (12.0)	5 (7.2)	7 (10.0)
Partial response	18 (12.3)	20 (16.1)	22 (11.8)	16 (19.3)	8 (11.6)	10 (14.3)
Stable disease	24 (16.4)	32 (25.8)	36 (19.3)	20 (24.1)	11 (15.9)	16 (22.9)
Progressive disease	71 (48.6)	40 (32.3)	87 (46.5)	24 (28.9)	37 (53.6)	24 (34.3)
Not evaluable	27 (18.5)	20 (16.1)	34 (18.2)	13 (15.7)	8 (11.6)	13 (18.6)

**Supplementary Table 2.** Treatment-related adverse events and treatment-related select AEs<sup>b</sup> in all treated patients

Preferred term, <i>n</i> (%)	All treated patients <i>N</i> = 270	
	Any grade	Grade 3–4 <sup>a</sup>
Total patients with a treatment-related AE	187 (69.3)	67 (24.8)
Treatment-related AEs in ≥5% of patients		
Fatigue	52 (19.3)	5 (1.9)
Diarrhea	35 (13.0)	8 (3.0)
Pruritus	32 (11.9)	0
Decreased appetite	26 (9.6)	0
Rash	24 (8.9)	4 (1.5)
Hypothyroidism	23 (8.5)	0
Nausea	21 (7.8)	1 (0.4)
Asthenia	19 (7.0)	5 (1.9)
Pyrexia	17 (6.3)	1 (0.4)
Lipase increased	15 (5.6)	13 (4.8)
Amylase increased	14 (5.2)	8 (3.0)
Treatment-related select AE category, <i>n</i> (%)		
Skin	64 (23.7)	8 (3.0)
Gastrointestinal	36 (13.3)	10 (3.7)
Hepatic	15 (5.6)	6 (2.2)
Pulmonary	14 (5.2)	4 (1.5) <sup>c</sup>
Renal	5 (1.9)	1 (0.4)

Endocrine		
Adrenal disorder	4 (1.5)	2 (0.7)
Diabetes	1 (0.4)	0
Pituitary disorder	2 (0.7)	1 (0.4)
Thyroid disorder	39 (14.4)	0

<sup>a</sup>Grade 5 treatment-related AEs occurred in 3 patients (1 instance each of pneumonitis, respiratory failure, and circulatory collapse).

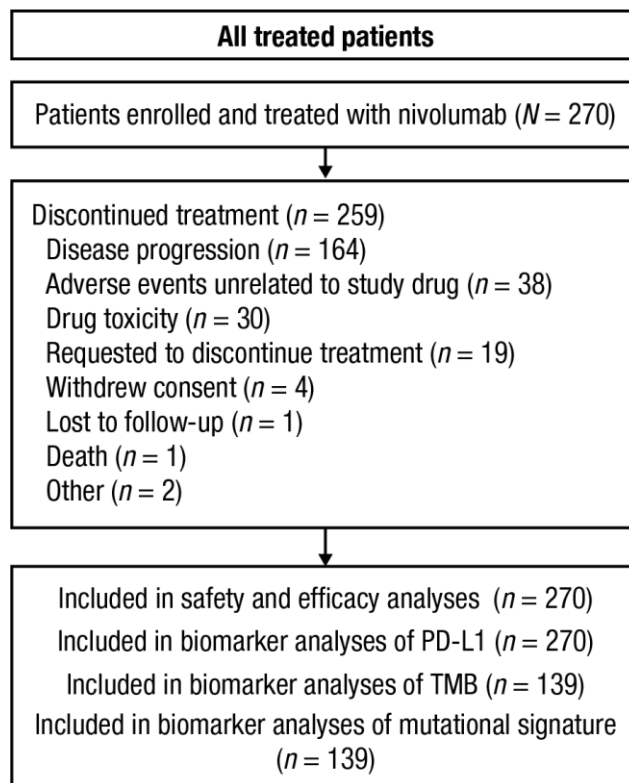
<sup>b</sup>Select AEs are those with a potential immunological cause.

<sup>c</sup>One grade 5 treatment-related select pulmonary AE occurred (pneumonitis); this event was previously reported (1).

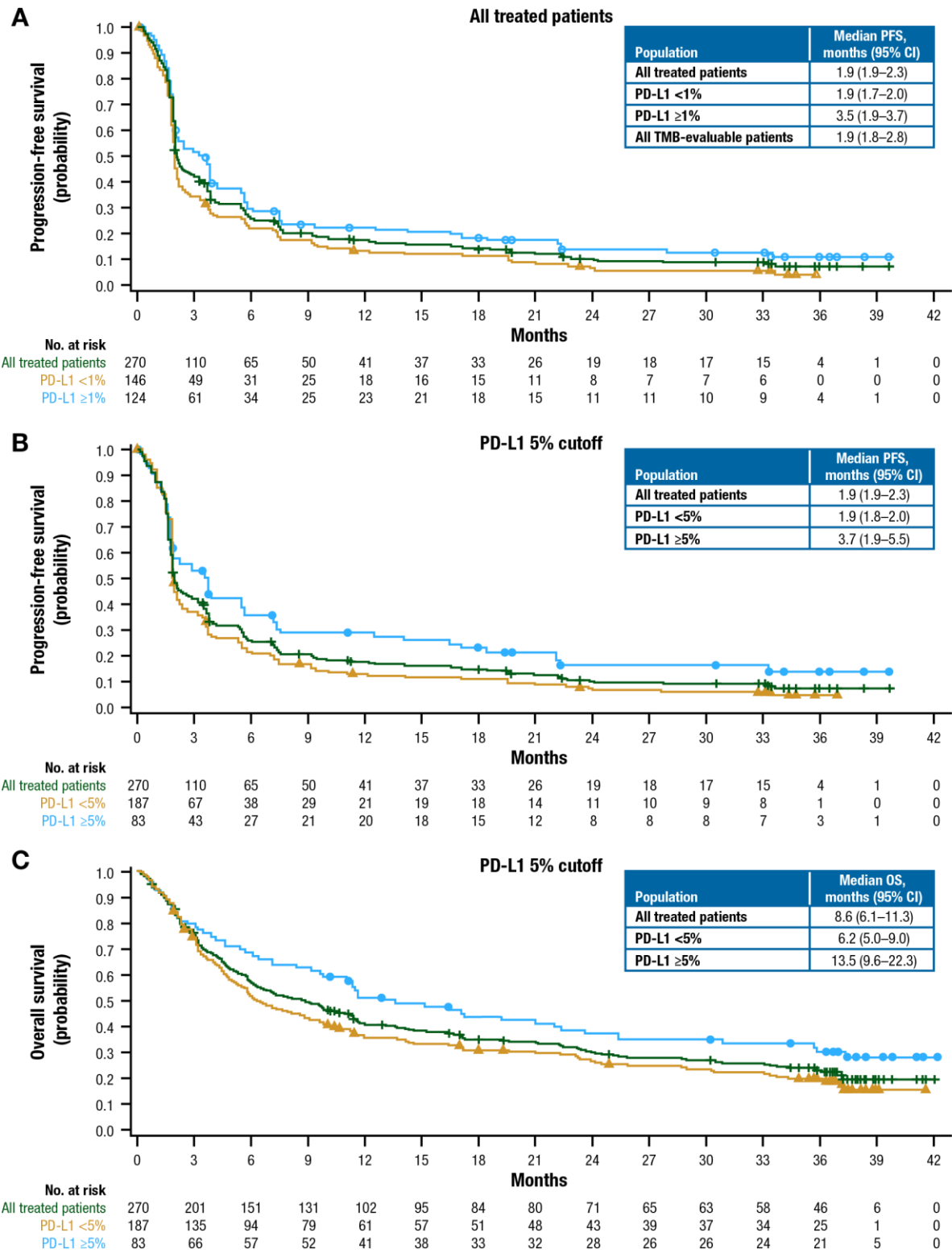
## Reference

1. Sharma P, Retz M, Siefker-Radtke A, et al. Nivolumab in metastatic urothelial carcinoma after platinum therapy (CheckMate 275): a multicentre, single-arm, phase 2 trial. *Lancet Oncol* 2017;18:312–22.

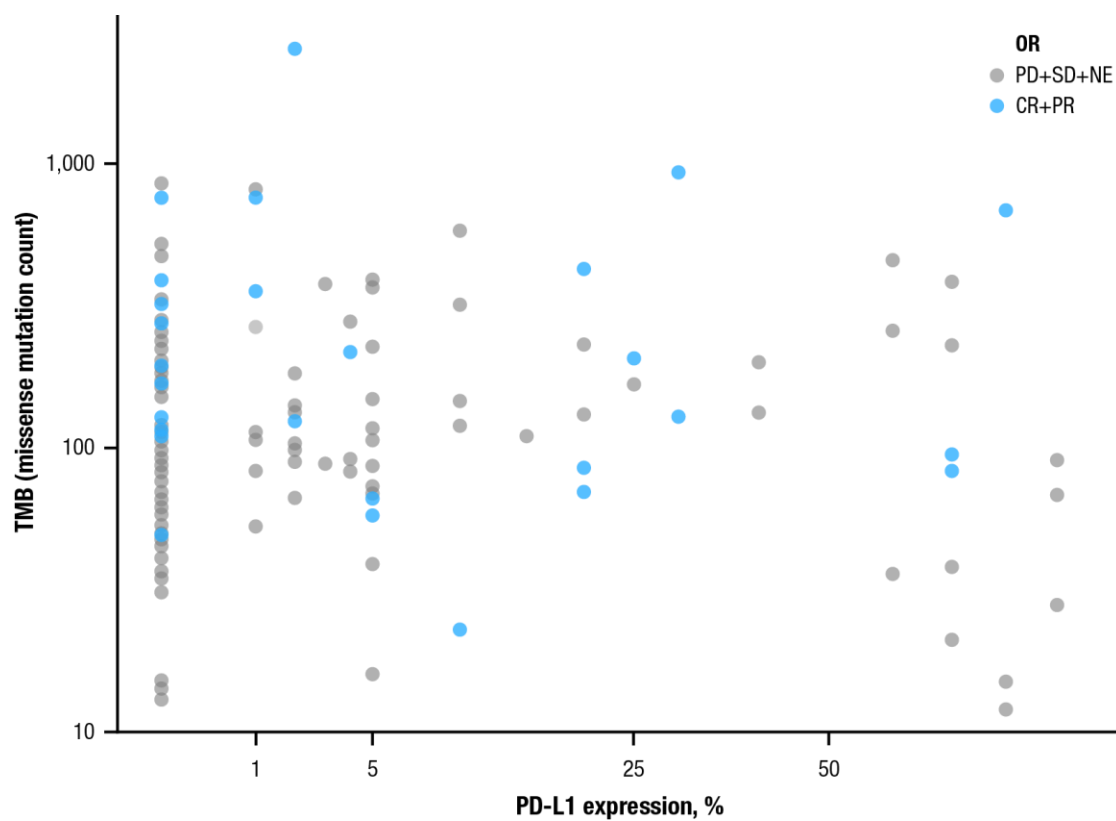
**Supplementary Figure 1.** CONSORT diagram.



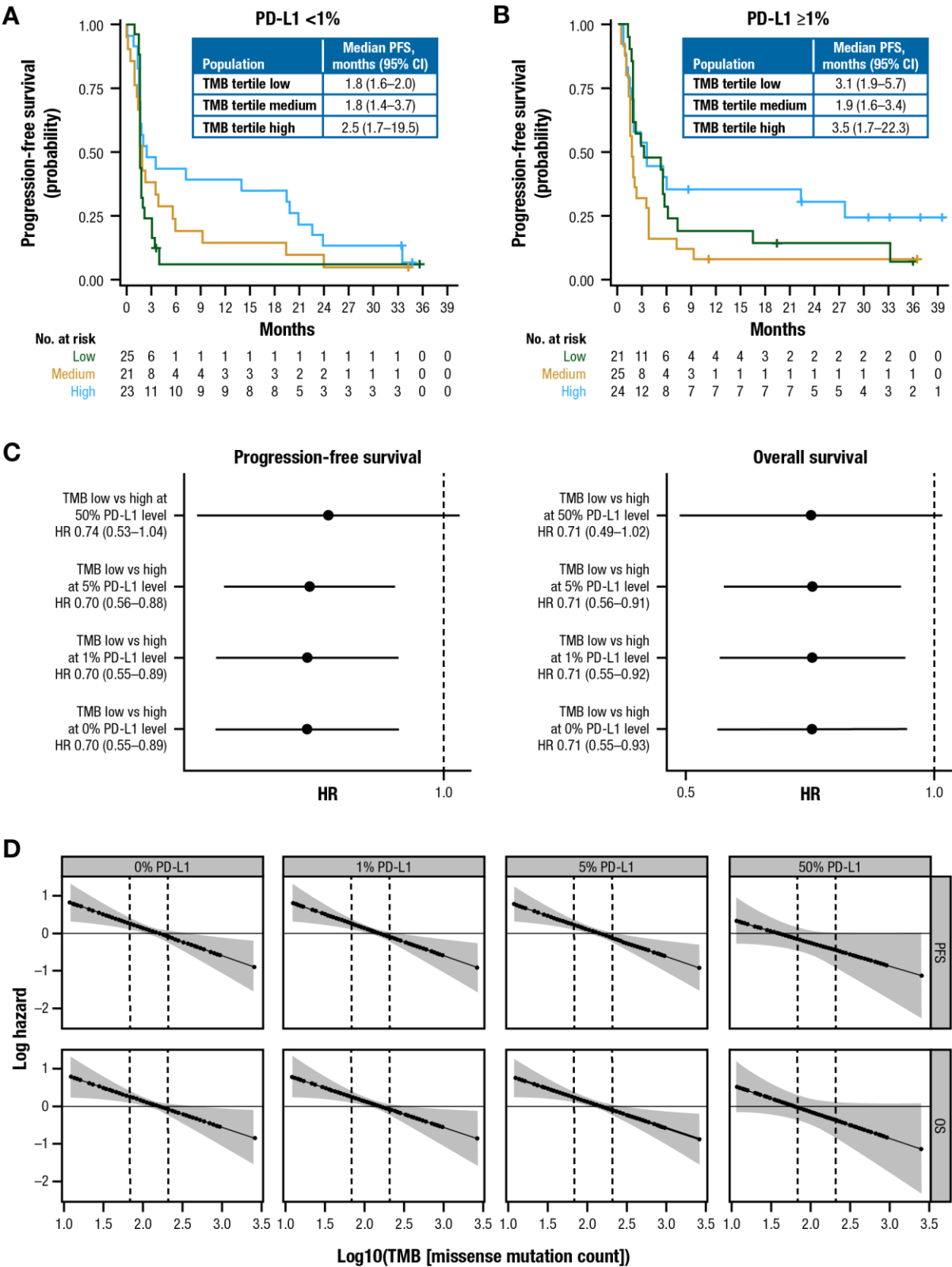
**Supplementary Figure 2.** PFS per BIRC in all treated patients and by PD-L1 expression (1% cutoff) **(A)** PFS per BIRC by PD-L1 expression (5% cutoff) **(B)** and OS per BIRC by PD-L1 expression (5% cutoff) **(C)**.



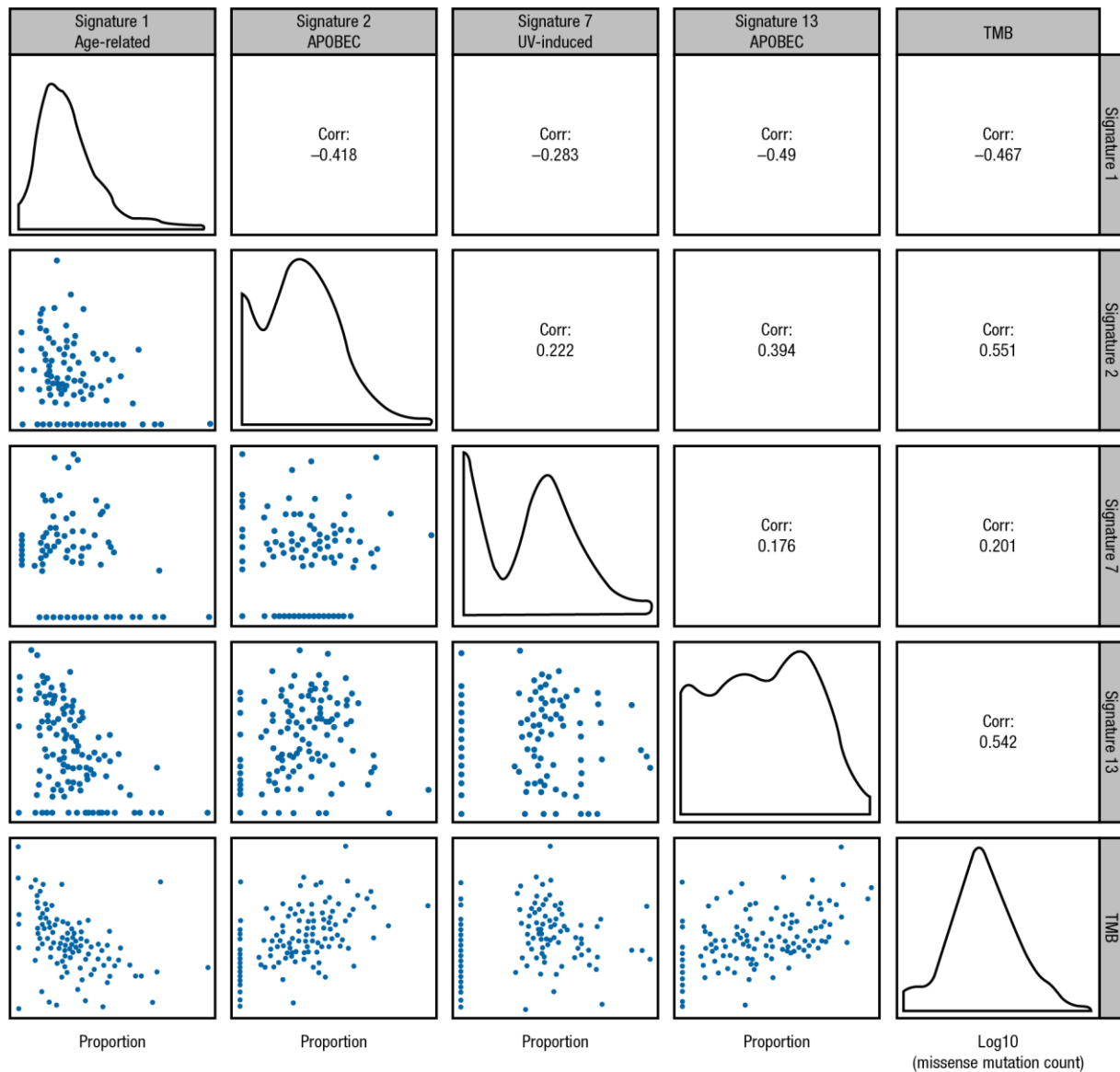
**Supplementary Figure 3.** Correlation of PD-L1 expression and TMB. Abbreviations: CR, complete response; NE, not evaluable; OR, overall response; PD, progressive disease; PR, partial response; SD, stable disease.



**Supplementary Figure 4.** PFS by TMB tertiles in patients with PD-L1 expression <1% **(A)** PFS by TMB tertiles in patients with PD-L1 expression ≥1% **(B)**. HR for PFS and OS for TMB according to PD-L1 levels **(C)** TMB log hazard at multiple PD-L1 levels **(D)**.



**Supplementary Figure 5.** Correlation of top mutational signatures with TMB. The lower triangle shows pairwise scatter plots for TMB and mutational signature scores. The upper triangle shows correlation coefficients for the corresponding scatter plots. Plots on the diagonal show density estimates for TMB and mutational signature scores.



**Supplementary Figure 6.** Association of mutational signature with PFS **(A)** objective response **(B)** best overall response **(C)** and OS **(D)**. Abbreviation: BOR, best overall response.

